PATENT
Customer No. 22,852
Attorney Docket No. 07586.0530-01

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re Application of:	)	
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Patrick Benoit *et al.*	)	Group Art Unit: 1635
	)	
Application No.: 10/802,030	)	Examiner: Terra C. Gibbs
	)	
Filed: March 17, 2004	)	
	)	
For: SEQUENCES UPSTREAM OF THE CARP GENE, VECTORS CONTAINING THEM AND USES THEREFORE	)	Confirmation No.: 3970

Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

Sir:

PETITION UNDER 37 C.F.R. §§ 1.144 AND 1.181
FOR WITHDRAWAL OF RESTRICTION REQUIREMENT

Pursuant to 37 C.F.R. § 1.144 and 37 C.F.R. § 1.181, Applicants respectfully petition the Commissioner to review the restriction requirement set forth in the Office Action mailed July 19, 2006 ("Restriction Requirement"). The restriction requirement was made final in the Office Action mailed October 19, 2006 ("Office Action"), at pp. 5.

The Examiner required restriction under 35 U.S.C. § 121 of the 21 pending claims among the following 16 groups:

> Group I. Claims 1, 2, 7, and 9-19, allegedly drawn to a polynucleotide comprising a fragment of SEQ ID NO: 3, or a fragment of a sequence that hybridizes under high stringency conditions to SEQ ID NO: 3, wherein said polynucleotide, in the absence of inverted terminal repeat sequences from AAV, specifically induces expression in cardiac cells *in vivo* of a gene which is

operably linked to said polynucleotide and an expression cassette comprising said polynucleotide, classifiable in class 536, subclass 24.5.

Group II. Claims 1, 2, 7, and 9-19, allegedly drawn to a polynucleotide comprising a fragment of SEQ ID NO: 4, or a fragment of a sequence that hybridizes under high stringency conditions to SEQ ID NO: 4, wherein said polynucleotide, in the absence of inverted terminal repeat sequences from AAV, specifically induces expression in cardiac cells *in vivo* of a gene which is operably linked to said polynucleotide and an expression cassette comprising said polynucleotide, classifiable in class 536, subclass 24.5.

Group III. Claims 1, 2, 7, and 9-19, allegedly drawn to a polynucleotide comprising a fragment of SEQ ID NO: 5, or a fragment of a sequence that hybridizes under high stringency conditions to SEQ ID NO:5, wherein said polynucleotide, in the absence of inverted terminal repeat sequences from AAV, specifically induces expression in cardiac cells *in vivo* of a gene which is operably linked to said polynucleotide and a vector comprising said polynucleotide, classifiable in class 536, subclass 24.5.

Group IV. Claims 1, 2, 7, and 9-19, allegedly drawn to a polynucleotide comprising a fragment of SEQ ID NO: 6, or a fragment of a sequence that hybridizes under high stringency conditions to SEQ ID NO: 6, wherein said polynucleotide, in the absence of inverted terminal repeat sequences from AAV, specifically induces expression in cardiac cells *in vivo* of a gene which is operably linked to said polynucleotide and an expression cassette comprising said polynucleotide, classifiable in class 536, subclass 24.5.

Group V. Claims 1, 2, 7, and 9-19, allegedly drawn to a polynucleotide comprising a fragment of SEQ ID N0: 7, or a fragment of a sequence that hybridizes under high stringency conditions to SEQ ID NO: 7, wherein said polynucleotide, in the absence of inverted terminal repeat sequences from AAV, specifically induces expression in cardiac cells *in vivo* of a gene which is operably linked to said polynucleotide and an expression cassette comprising

said polynucleotide, classifiable in class 536, subclass 24.5.

Group VI. Claims 1, 7, and 8, allegedly drawn to an expression cassette comprising a polynucleotide comprising a fragment of SEQ ID NO: 3, or a fragment of a sequence that hybridizes under high stringency conditions to SEQ ID NO: 3, wherein said polynucleotide, in the absence of inverted terminal repeat sequences from AAV, specifically induces expression in cardiac cells *in vivo* of a gene which is operably linked to said polynucleotide and further comprising SEQ ID NO: 9, classifiable in class 536, subclass 24.5.

Group VII. Claims 1, 7, and 8, allegedly drawn to an expression cassette comprising a polynucleotide comprising a fragment of SEQ ID NO: 4, or a fragment of a sequence that hybridizes under high stringency conditions to SEQ ID NO: 4, wherein said polynucleotide, in the absence of inverted terminal repeat sequences from AAV, specifically induces expression in cardiac cells *in vivo* of a gene which is operably linked to said polynucleotide and further comprising SEQ ID NO: 9, classifiable in class 536, subclass 24.5.

Group VIII. Claims I,7, and 8, allegedly drawn to an expression cassette comprising a polynucleotide comprising a fragment of SEQ ID NO: 5, or a fragment of a sequence that hybridizes under high stringency conditions to SEQ ID NO: 5, wherein said polynucleotide, in the absence of inverted terminal repeat sequences from AAV, specifically induces expression in cardiac cells *in vivo* of a gene which is operably linked to said polynucleotide and further comprising SEQ ID NO: 9, classifiable in class 536, subclass 24.5.

Group IX. Claims 1, 7, and 8, allegedly drawn to an expression cassette comprising a polynucleotide comprising a fragment of SEQ ID NO: 6, or a fragment of a sequence that hybridizes under high stringency conditions to SEQ ID NO: 6, wherein said polynucleotide, in the absence of inverted terminal repeat sequences from AAV, specifically induces expression in cardiac cells *in vivo* of a gene which is operably linked to said polynucleotide and further comprising SEQ ID NO: 9, classifiable in class 536, subclass 24.5.

Group X. Claims 1, 7, and 8, allegedly drawn to an expression cassette comprising a polynucleotide comprising a fragment of SEQ ID NO: 7, or a fragment of a sequence that hybridizes under high stringency conditions to SEQ ID NO: 7, wherein said polynucleotide, in the absence of inverted terminal repeat sequences from AAV, specifically induces expression in cardiac cells *in vivo* of a gene which is operably linked to said polynucleotide and further comprising SEQ ID NO: 9, classifiable in class 536, subclass 24.5.

Group XI. Claim 20, allegedly drawn to a method for expressing a protein or an RNA of therapeutic interest in cardiac cells *in vivo*, comprising preparing and introducing into cells an expression cassette comprising a polynucleotide comprising a fragment of SEQ ID NO: 3, or a fragment of a sequence that hybridizes under high stringency conditions to SEQ ID NO: 3, wherein said polynucleotide, in the absence of inverted terminal repeat sequences from AAV, specifically induces expression in cardiac cells *in vivo* of a gene which is operably linked to said polynucleotide, classifiable in class 435, subclass 91.1.

Group XII. Claim 20, allegedly drawn to a method for expressing a protein or an RNA of therapeutic interest in cardiac cells *in vivo,* comprising preparing and introducing into cells an expression cassette comprising a polynucleotide comprising a fragment of SEQ ID NO: 4, or a fragment of a sequence that hybridizes under high stringency conditions to SEQ ID NO: 4, wherein said polynucleotide, in the absence of inverted terminal repeat sequences from AAV, specifically induces expression in cardiac cells *in vivo* of a gene which is operably linked to said polynucleotide, classifiable in class 435, subclass 91.1.

Group XIII. Claim 20, allegedly drawn to a method for expressing a protein or an RNA of therapeutic interest in cardiac cells *in vivo,* comprising preparing and introducing into cells an expression cassette comprising a polynucleotide comprising a fragment of SEQ ID NO: 5, or a fragment of a sequence that hybridizes under high stringency conditions to SEQ ID NO: 5, wherein said polynucleotide, in the absence of inverted terminal repeat sequences from AAV,

specifically induces expression in cardiac cells *in vivo* of a gene which is operably linked to said polynucleotide, classifiable in class 435, subclass 91.1.

Group XIV. Claim 20, allegedly drawn to a method for expressing a protein or an RNA of therapeutic interest in cardiac cells *in vivo*, comprising preparing and introducing into cells an expression cassette comprising a polynucleotide comprising a fragment of SEQ ID N0: 6, or a fragment of a sequence that hybridizes under high stringency conditions to SEQ ID NO: 6, wherein said polynucleotide, in the absence of inverted terminal repeat sequences from AAV, specifically induces expression in cardiac cells *in vivo* of a gene which is operably linked to said polynucleotide, classifiable in class 435, subclass 91.1.

Group XV. Claim 20, allegedly drawn to a method for expressing a protein or an RNA of therapeutic interest in cardiac cells *in vivo*, comprising preparing and introducing into cells an expression cassette comprising a polynucleotide comprising a fragment of SEQ ID NO: 7, or a fragment of a sequence that hybridizes under high stringency conditions to SEQ ID NO: 7, wherein said polynucleotide, in the absence of inverted terminal repeat sequences from AAV, specifically induces expression in cardiac cells *in vivo* of a gene which is operably linked to said polynucleotide, classifiable in class 435, subclass 91.1.

Group XVI. Claim 21, allegedly drawn to a polynucleotide comprising a fragment of SEQ ID NO: 2 or a fragment having at least 80% sequence identity to a fragment of SEQ ID NO: 2, wherein said fragment is at least 77 nucleotides in length and wherein said polynucleotide, in the absence of inverted terminal repeat sequences from AAV, specifically induces expression in cardiac cells *in vivo* of a gene which is operably linked to said polynucleotide, classifiable in class 536, subclass 24.1.

Restriction Requirement, 7/19/06, pages 2-7.

A. A Search of the Prior Art Related to the Claimed Sequences Does Not Constitute an Undue Burden on the Examiner

The Examiner acknowledges that Groups I-X are related to each other because they are drawn to related polynucleotides. *Id.* at 4. Nevertheless, the Examiner asserts that restriction is proper because each Group "employs different molecules with different chemical properties and physical structures so that independent searches of the prior art would be required that would constitute a serious burden on the Examiner." Office Action, July 19, 2006, pp. 9-10. The Examiner claims that a search of the polynucleotides of Groups I and II, would not encompass all of the art relevant to the polynucleotides of Groups II-V. *Id.* at 9.

Moreover, the Examiner asserts that a search of the polynucleotide of Group III, would not encompass all of the art relevant to the polynucleotides of Groups IV and V. The Examiner also claims that searching the inventions of Groups I-V together with Groups VI-X "would impose a serious search burden." *Id.* at 10. In addition, the Examiner asserts that a polynucleotide comprising a fragment of SEQ ID NO: 2 or a fragment having at least 80% sequence identity to a fragment of SEQ ID NO: 2, wherein said fragment is at least 77 nucleotides in length, and wherein said polynucleotide in the absence of inverted terminal repeat sequences from human adeno-associated virus specifically induces expression in cardiac cells *in vivo* of a gene which is operably linked to said polynucleotide, is a polynucleotide not found in any other Group. *Id.* at 10.

Applicants responded to the Restriction Requirement by electing Group I with traverse. Response to Restriction Requirement, August 8, 2006, pp. 5-8. In

responding, Applicants cited the relevant portion of the M.P.E.P. regarding searches of sequences:

> . . . each such nucleotide sequence is presumed to represent an independent and distinct invention, subject to a restriction requirement pursuant to 35 U.S.C. 121 and 37 CFR 1.141 et seq. Nevertheless, to further aid the biotechnology industry in protecting its intellectual property without creating an undue burden on the Office, the Commissioner has decided sua sponte to partially waive the requirements of 37 CFR 1.141 et seq. and permit a reasonable number of such nucleotide sequences to be claimed in a single application. See Examination of Patent Applications Containing Nucleotide Sequences, 1192 O.G. 68 (November 19, 1996).

M.P.E.P. § 803.04.

Applicants further cited the M.P.E.P., which states that "in most cases, up to ten independent and distinct nucleotide sequences will be examined in a single application without restriction." *Id.* As noted by Applicants, there are six nested sequences, corresponding to SEQ ID NOs: 2-7, and a ninth sequence, SEQ ID NO: 9.

In the Office Action mailed October 10, 2006, the Examiner did not consider Applicant's arguments persuasive because "such guidelines issued in 1996, and the size of the nucleotide sequence database has doubled approximately very six months since then. Thus, the number of returned hits for nucleotide sequence searches has expanded dramatically since the time the guidelines were issued." Office Action, p. 2. The Examiner concluded that analysis of the search results "is considered to constitute a serious burden." *Id.* at 3.

Applicants respectfully submit that restriction between inventions classified as Groups I-X and XVI conflicts with the Commissioner's decision as embodied in M.P.E.P.

§ 803.04. It goes without stating that an Examiner is not free to disregard the Commissioner's decision. Moreover, the Examiner required restriction between inventions encompassing nested sequences derived from the same complete sequence, the human CARP gene. The M.P.E.P states that "up to ten **independent and distinct** nucleotide sequences will be examined in a single application. M.P.E.P. § 803.04 (emphasis added). SEQ ID NOs: 3-7 are not independent and distinct, but are subsequences of each other. Applicants are sympathetic to the burden on an Examiner of searching ten independent and distinct sequences. However, a proper evaluation of the claimed sequences does not require such a search.

Applicants submit that a search of the human CARP gene would encompass SEQ ID NOs: 2-7, and that a search for the smallest fragment of the nested fragments claimed would reveal all prior art related to each of SEQ ID NOs: 2-7 since each of these sequences **contains** the smallest subsequence. Moreover, the sequence of the fragment of the human cardiac α-actin promoter (SEQ ID NO: 9) was known prior to this application and is only part of the invention in conjunction with SEQ ID NOs: 2-7. A search of the prior art for SEQ ID NOs: 2-7 would also reveal if any of these CARP sequences were used in conjunction with a fragment of the human cardiac α-actin promoter. Thus, no additional searching is required.

B. The Restriction Requirement was in Improper Restriction Among Members of a Markush Group

The Examiner improperly required restriction between members of a Markush group. As stated by the M.P.E.P, "[s]ince the decisions in *In re Weber*, 580 F.2d 455, 198 USPQ 328 (CCPA 1978) and *In re Haas*, 580 F.2d 461, 198 USPQ 334 (CCPA

1978), it is improper for the Office to refuse to examine that which applicants regard as their invention, unless the subject matter in a claim lacks unity of invention." M.P.E.P 803.02 (quoting *In re Harnisch*, 631 F.2d 716, 206 USPQ 300 (CCPA 1980); and *Ex parte Hozumi*, 3 USPQ2d 1059 (Bd. Pat. App. & Int. 1984)). Unity of invention exists where "compounds included within a Markush group (1) share a common utility, and (2) share a substantial structural feature essential to that utility." *Id.* The claims recite polynucleotides in the absence of inverted terminal repeat sequences from adeno-associated virus which specifically induce expression in cardiac cells *in vivo* of a gene which is operably linked to said polynucleotide. The claimed sequences share this common utility, and, because they are nested sequences, they share features essential to this utility. Accordingly, it was improper to require restriction among these polynucleotide sequences.

CONCLUSION

In view of the foregoing remarks, Applicants respectfully request that the Commissioner grant Applicants' request and withdraw the restriction requirement.

Please grant any extensions of time required to enter this Petition and charge any additional required fees to our Deposit Account No. 06-0916.

Respectfully submitted,

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Date: January 23, 2007